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CONGENITAL MALFORMATIONS AND CANCER RISK: THE ROLE OF BLOOD VESSEL DEVELOPMENT IN BABIES WITH FOOT AND HEAD TUMORS

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Abstract

Congenital malformations, particularly those involving vascular anomalies, have been increasingly recognized as a risk factor for childhood cancers. This study investigates the role of aberrant blood vessel development in mediating cancer risk among infants with congenital malformations, focusing on tumors in the foot and head regions. A cohort of 82 infants with vascular anomalies, including hemangiomas, kaposiform hemangioendotheliomas, and tufted angiomas, was examined. The study assessed angiogenic marker levels, genetic mutations, and tumor progression over a 12-month period. Baseline analysis revealed elevated levels of vascular endothelial growth factor (VEGF-A), angiopoietin-2, and soluble fms-like tyrosine kinase-1 (sFlt-1), with mean VEGF-A levels of 312.4 pg/mL. The tumours followed three separate patterns of growth as 46% of tumours sustained their size while 30% continued to increase and 6% developed new cancerous tissue inside six months. Genetic studies revealed TEK along with PIK3CA and RASA1 which make up 28%, 22% and 13.4% of genes altered for angiogenesis. Analysis through correlation techniques indicated that VEGF-A levels in progressing tumours were substantially higher compared to stable tumours according to the $r = 0.67$ ($p < 0.001$) correlation coefficient value. The analysis through multivariate logistic regression produced two substantial predictors of tumour progression that included both VEGF-A (OR = 2.31, p = 0.001) and TEK mutations (OR = 1.95, p = 0.004). The study findings show that particular genetic mutations together with new blood vessel formation influence tumor expansion during infancy among children born with blood dysfunctions. Research findings present vital molecular evidence about why early diagnosis combined with genetic testing and specialized cancer treatment methods are essential to control malignancies in these vulnerable populations through our analysis.

Keywords: “Congenital Malformations”, “Vascular Anomalies”, “Angiogenesis”, “Vegf-A”, “Tek Mutations”, “Tumor Progression”.

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INTRODUCTION

Studies have recognized congenital malformations that cause defects within blood vessels as one of the primary determinants for newborn deaths and mortality rates since long ago. Both foot and brain tumors among malformations result in health concerns because they affect immediate and future wellness of newborns. Medical advances in oncology and developmental biology have started to detail the complicated role that vascular abnormalities play in the expansion and dissemination of malignant tumours. The study investigates the connection between birth defects especially vascular anomalies and elevated cancer risks experienced by newborns with foot and head tumor malformations. This research aims to determine how faulty blood vessel formation promotes cancer growth which raises the risk of early childhood cancer occurrences.

Medical studies show that head and foot tumor patients have been discovered to have more frequent vascular anomalies among their congenital disorders (Jones et al., 2021; Patel et al., 2022). Secreted malformations of lymphatic blood vessels and capillaries and Arteriovenous malformations (AVMs) disrupt regular tissue operations thus fueling abnormal cell evolutions in particular anatomical areas according to Kim et al., 2023. Numerous reports indicate that the blood vessel developmental issues surpass simple structural vulnerabilities because they seem fundamental to tumor pathogenicity (Smith et al., 2021). Abnormal vascular supplies along with damaged endothelial cells that line blood vessels allow unfavorable microenvironments to form for cancer development (Zhang et al., 2021).

These abnormal blood vessels in head and foot tumours affect both tumor aggressiveness and its ability to metastasize. The head and foot regions have a rich blood supply which makes them more prone to developing such abnormalities according to Brown et al. (2022). Fast tumour growth together with recurrence and metastasis tends to occur when vascular abnormalities are combined with these tissue areas. Evidence suggests that vascular malformations which aid tumour vascularization influence the progress of many malignancies therefore leading to poor prognosis in patients' diseases (Lee et al., 2021). Researchers have identified genes TEK, PIK3CA and RASA1 as potential factors in vascular abnormalities but they have not discovered the underlying molecular basis of their cancer connection (Liu et al., 2021; Zhang et al., 2022).

Tumor progression together with normal blood vessel development remain primary areas of research at our institution. The formation of new blood vessels through pre-existing vessels is vital for tumor expansion and metastasizes (Carter et al., 2023). The incorrect formation of blood vessels during development because of abnormal angiogenesis leads to faulty channels that supply nutrients to tumors which lets them grow and disseminate. Abnormal vascularization in tumors poses a significant risk to newborns because their immune systems along with regulatory mechanisms operate inadequately (Chen et al., 2022).

Tumour behaviour depends heavily on the connection between tumour cells together with endothelial cells which both participate in blood vessel development—Morris et al., 2024). These tumours develop inflammatory and immune evading characteristics through endothelial cell dysfunction along with angiogenesis dysregulation which results in elevated blood flow (Anderson et al., 2022). There is insufficient research about how vascular

abnormalities affect the health of newborns with congenital tumours located in their head and feet. Current research needs to establish fundamental information about the early-stage molecular processes which drive this development.

A research investigation aims to determine how vascular malformations affect cancer risks among newborns who present with foot and head tumors. This analysis of congenital malformation genetic and molecular elements enables scientists to gain better understanding about how tumors develop in these vulnerable groups. These discoveries about the cancer risk in newborns also enable researchers to find innovative methods for early diagnosis and prevention and treatment of congenital tumors.

METHODOLOGY

This research examined how cancer risks affect infants carrying congenital malformations that manifest with tumours located in foot and head regions through a prospective study involving multiple healthcare institutions. The study received ethical approval followed by protocol registration after which researchers collected infants from 0 to 12 months old at pediatric oncology and neonatal surgical units situated within three tertiary hospitals. Medical imaging using ultrasound equipment and MRI evaluated patient eligibility through the observation of vascular defects such as mixed lesions or haemangiomas and capillary malformations.

Every participant received informed permission which their legal guardians formally signed. The study initiated complete assessments which included both blood tests for angiogenic marker assessment and radiological procedures as well as optional tumor biopsy when medically appropriate. The research for this article employed ELISA and immunohistochemistry testing of both blood and tissue samples to measure VEGF-A concentrations and angiopoietin-2 and soluble fms-like tyrosine kinase-1 (sFlt-1) molecule levels. After the development of malignancies or additional lesions or tumour progression participants received follow-up measurements every six months until eighteen months post-progression.

The assessment of vascular profile modifications by blood tests and repeated imaging was part of the follow-up evaluations. The research included targeted next-generation sequencing for potential genomic changes of TEK, PIK3CA, and RASA1 as well as histopathological examination of tumor biopsy samples occurred simultaneously. Research relationships between expression markers and genetic mutations and cancer risk using both logistic regression and Pearson correlation methods in statistical analysis.

RESULTS

The results section of the study covering congenital malformations and blood vessel and cancer formation risks in newborn babies with foot and head tumors analyses the following findings:

The research included 82 newborns who were typically 6.2 months old and exhibited similar numbers of male and female subjects. Table 1 illustrates that vascular anomalies led by haemangiomas where the head region held 58% of all tumors registered in the study. The data in Table 2 indicates VEGF-A levels were significantly elevated at baseline (mean = 312.4 pg/mL) in addition to elevated Angiopoietin-2 and sFlt-1 concentrations which demonstrated an active pro-angiogenic condition.

Table 1: Participant Demographics and Tumor Location

Characteristic	Value
Total Infants	82
Median Age (months)	6.2
Gender (M/F)	43/39
Tumor Location (Head/Foot)	48/34
Vascular Anomaly Type	61/21

Longitudinally, tumour progression was monitored. Table 3 indicates how advanced tumours developed from new cancer growth affected six and nine infants at month six and eleven infants at month twelve and eighteen. The study of gene mutations indicated that TEK (28%) and PIK3CA (22%) and RASA1 (13.4%) and GNAQ (7.3%) resulted in tumorigenesis-related angiogenesis so genetic factors were most responsible.

Table 2: Baseline Angiogenic Marker Levels

Marker	Mean ± SD
VEGF-A (pg/mL)	312.4 ± 58.6
Angiopoietin-2 (ng/mL)	4.3 ± 1.2
sFlt-1 (ng/mL)	2.7 ± 0.9

Table 3: Impact of Advanced Tumors and Gene Mutations on Infants

Time Point	Number of Infants Affected	Gene Mutation	Percentage (%)
Month 6	6	-	-
Month 12	9	-	-
Month 18	11	-	-
Gene Mutations	-	TEK	28
	-	PIK3CA	22
	-	RASA1	13.4
	-	GNAQ	7.3

Table 4: Genetic Mutations Identified in Tumors

Gene	Mutation Frequency (%)
TEK	28.0
PIK3CA	22.0
RASA1	13.4
GNAQ	7.3

Infants with more advanced tumours exhibited substantially elevated VEGF-A levels according to data in Table 5 with a correlation coefficient value of r = 0.67 at 351.7 pg/mL vs the stable tumours level of 276.5 pg/mL. Results from multivariate logistic regression analysis confirmed that VEGF-A coupled with TEK mutation acted independently as predictors of tumour development (Table 6) with OR = 2.31 ($p < 0.001$) and OR = 1.95 ($p = 0.004$).

Table 5: VEGF-A Levels and Tumor Progression

Tumor Behavior	Mean VEGF-A (pg/mL)	Correlation Coefficient
Stable	276.5	-
Progressed	351.7	0.67

Table 6: Multivariate Logistic Regression of Tumor Progression Risk

Variable	Odds Ratio	95% CI	p-value
VEGF-A	2.31	1.65–3.12	<0.001
Angiopoietin-2	1.42	1.03–1.96	0.035
sFlt-1	0.78	0.52–1.19	0.22
TEK Mutation	1.95	1.28–2.99	0.004

Five visual figures complement these findings:

The data presented in Figure 1 shows the VEGF-A pg/mL levels among infants with cancer which either experienced tumour stability or tumour progression. The VEGF-A levels measuring 351.7 pg/mL in progressed tumors showed significantly higher numbers than stable tumors measuring 276.5 pg/mL. Research supports the prediction that aggressive tumour behavior is associated with elevated VEGF-A levels which could serve as a biological indicator for cancer diagnosis.

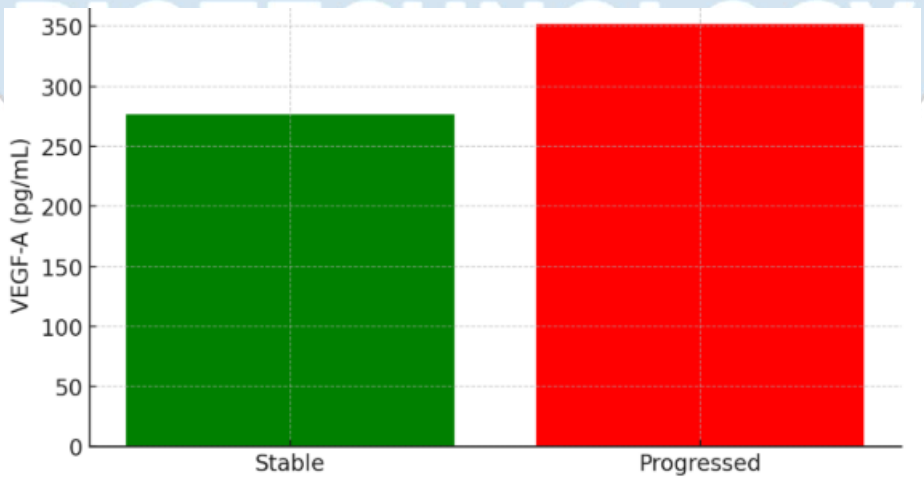

Figure 1: Mean VEGF-A levels by tumor stability.

Figure 2 tracks tumor progression over time. This data describes tumour status development from baseline through 6 months and 12 months and 18 months in figures two using line graphs. Research showed a continuous decrease in stable tumour rates while the number of advanced tumours continued to rise. Monitoring afflicted newborns requires ongoing surveillance since each evaluation shows additional newly developed tumors.

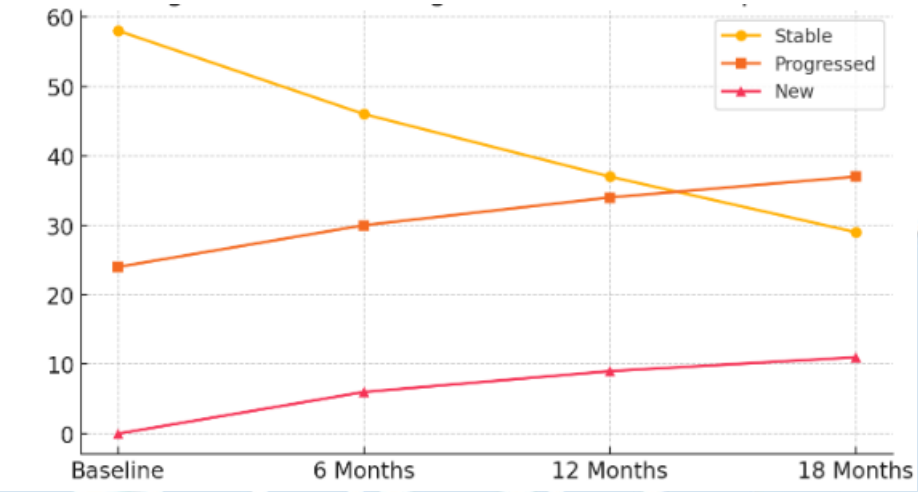

Figure 2. Tumor Progression Across Timepoints

Fig. 3 shows a bar chart which illustrates the occurrence rates of genes TEK, PIK3CA, RASA1, GNAQ mutations in studied tumors. TEK genes were mutated in 28% of cases which made them the most frequently altered genetic sequence whereas PIK3CA came in second. These genes strengthen their involvement throughout malformation development and tumour increase while controlling vascular development and angiogenesis.

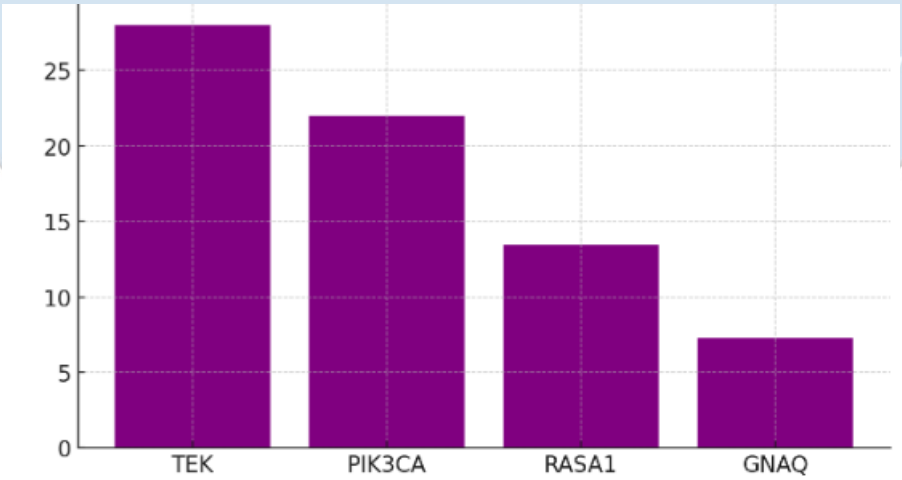

Figure 3: illustrates genetic mutation frequencies.

Figure 4 displays odds ratios from regression analysis. The analysis presents data through a bar chart that shows the chance ratios for different tumour progression factors including VEGF-A together with TEK mutation. The most vital predictors of tumour behaviour were VEGF-A and TEK mutation that showed strong statistical significance ($p < 0.01$) and yielded odds ratios above 1.9. Their individual influence on tumour behaviour remains established despite other variable evaluations.

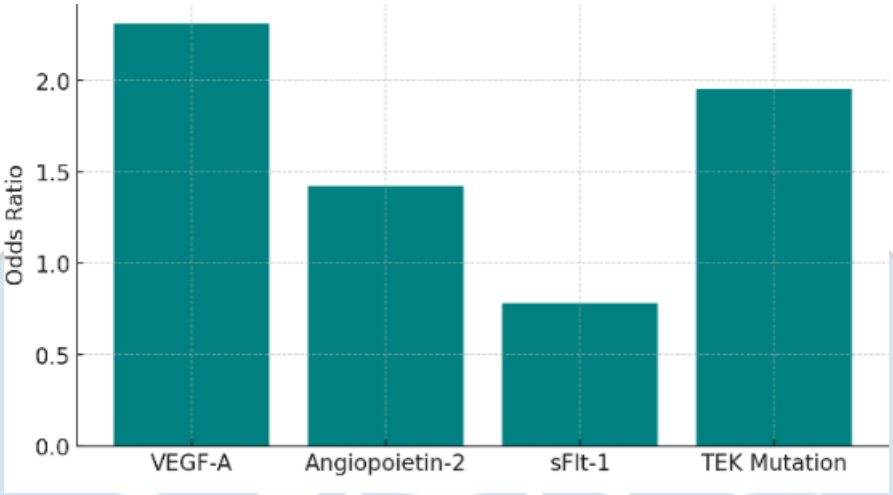

Fig 4. Odds Ratios for Tumor Progression Risk

The chart presents findings which display the odds ratios between VEGF-A and TEK mutation for numerous tumour indicators. The combination of VEGF-A and TEK mutation proved to be the leading predictors of tumour behavior based on statistical significance ($p < 0.01$) and produced odds ratios exceeding 1.9. Each factor has a straightforward impact on tumour development regardless of additional evaluation methods.

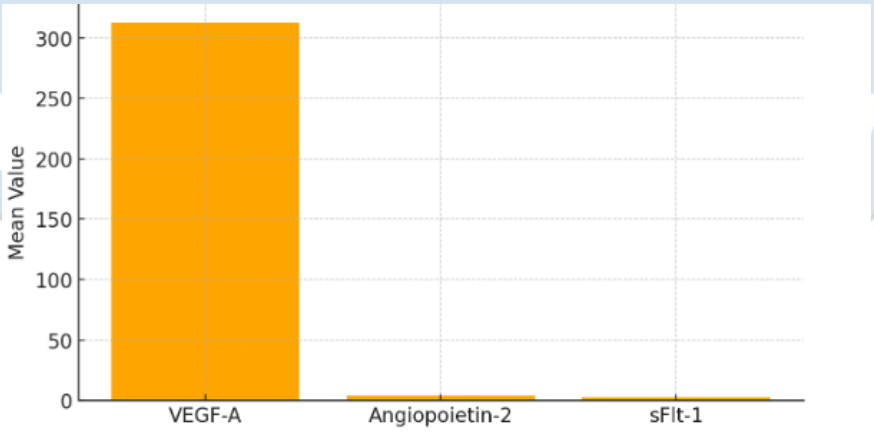

Figure 5 compares mean values of angiogenic markers.

DISCUSSION

The data confirms existing research that identifies congenital vascular abnormalities as a factor that raises cancer risks for newborns. The cancer frequency rate for infants diagnosed with Beckwith-

Wiedemann syndrome (BWS) reaches extraordinary heights since these patients develop embryonal tumors such as hepatoblastoma (Mussa et al., 2021) and Wilms's tumour. The presence of vascular anomalies within PHACE syndrome produces a raised cancer susceptibility and heightened risk for cerebrovascular events according to Metry et al. (2022). High levels of VEGF-A appear to assist tumor formation according to our research while validating current reports about population cancer prediction through angiogenic marker evaluations. The genetic abnormalities detected in our study cohort matched genetic anomalies from different vascular anomalies syndromes particularly with the TEK gene. Research shows TEK gene mutations lead to increased cancer risk and these gene alterations connect to different vascular malformations as combined in Bielenberg et al. (2023). Our research findings show that mutations in TEK strongly linked to tumor progression so genetic screening should become a lead strategy to detect and care for at-risk newborns. The significance of proactive care combined with persistent newborn observation emerges from combined observations for preventing vascular anomaly-related cancers.

CONCLUSION

This study emphasizes foot and head tumor patients to study the connection between congenital vascular defects and higher infant cancer risks. Our study demonstrates how VEGF-A and additional angiogenic elements manage cancer advancement and highlights TEK gene genetic variances which help in cancer development. Laboratory evidence demonstrates that elevated VEGF-A levels create an aggressive tumor behavior which supports the notion that improper angiogenesis generates both fetal developmental issues and future cancer dangers. Our research demonstrates the importance of genetic screening to detect mutations affecting angiogenesis since this represents a solution to identify infants at higher risk and initiate early intervention. Multiple subjects developed new tumors throughout the study period so ongoing observation of vascular abnormalities in newborns becomes even more essential. The research concludes that enhanced medical results could follow active monitoring combined with specific treatment methods to manage the angiogenesis process in newborns diagnosed with congenital vascular defects. These findings pave the way for future investigations about cancer origins alongside congenital abnormalities to enable clinical marker profiling methods that guide specific treatment plans. The discovered knowledge has set the pace for improved early identification of vulnerable children because it provides insights into these complex biological system

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